REMARKS

Claims 1 through 21 continue to be in the case.

New claims 22 through 29 are being submitted.

Claims 8, 13, 16, and 20 are being amended to conform to the requirements stated in point 12 of the Office Action of November 7, 2002.

The new claims have the following basis

New claim:	Basis
22	claim 13
23	claim 13
24	claim 1
25	specification, page 9, line 5
26	specification, page 5, lines 18 and 19
27	claim 17
28	specification page 9, line 5
29	specification, page 5, lines 18 and 19.

Applicants' attorney sincerely appreciates the personal interview kindly granted by Examiner David Isabella on March 18, 2003. The courtesies exchanged during the interview are very much appreciated.

During the interview applicants' attorney emphasized that the shear forces employed according to the present invention are clearly outside the range of shear forces present under the conditions of the Chamberlain reference. It was further pointed out that the applicants' process yield a product of much higher quality. Claim language was considered, which would distinguish the present inventionover the Chamberlain reference.

The Office Action of November 7, 2002 states as follows:

11. Claim 17 is indefinite because it is unclear what each of the method steps required are, as opposed to the processes that will naturally occur. Examiner suggests rewording the claim clearly pointing out what each of the method steps are.

It was kindly agreed during the personal interview that this rejection would be withdrawn.

New claim 27 is provided with the intention to lay out the method steps of claim 17 in a perhaps more clear fashion.

12. Claims 8, 13, 16 and 20 should be rewritten following the Markush format for listing of elements.

The present amendment rewrites claims 8, 13, 16 and 20 to furnish the format mentioned in the Office Action.

The Office Action refers to Claim Rejections - 35 USC § 102.

14. Claims 1-21 stand rejected under 35 U.S.C. 102(a) as being anticipated by Chamberlain (WO 93/01843).

Chamberlain according to the Office Action discloses a cardiovascular prosthesis with an initial sub-confluent seeding of endothelial cells on the surface thereof then forming a confluent monolayer of endothelial cells, with all the elements of claim 1. See page 11, lines 1-13 and abstract.

The shearing forces recited in the reference Chamberlain have only a small value. Only an area covering seeding is possible therewith. The growth of the cells cannot be influenced therewith. Thus no growth of cells occurred under shearing stress according to the Chamberlain reference. Claim 1 of the reference Chamberlain recites: " to cause the cells to become confluent and flatten ...". With this language reference is meant only the adherence of the cells for reaching of confluence as is clearly shown in the example presented in the reference Chamberlain: the cell suspension is subdivided into four aliquots and accordingly employed four times successively for coating. The risk of a non-face covering seeding is circumvented by this multiple step process. This is again confirmed on page 8 of the Chamberlain reference, where the remaining of the fourth aliquot in the prosthesis overnight, where

however the incubation overnight is described as dispensable for production of a confluent mono layer in paragraph 4 on page 8 of the Chamberlain reference. This corresponds to the initial confluent settling, wherein therewith a growth of the cells and an adaptation to the shearing stress, which shearing stress here is only smaller and thereby entered in a unphysiological size, is excluded in the proliferation process.

The reference Chamberlain further recites on page 8 paragraph 3 that a confluent, however not completely stable endothel cell mono layer is created, since partial cell disengagements occur. Therefore the product required according to claim one of the present application is clearly distinguished from the product described the Chamberlain reference.

Applicants specification recites on page, 5, lines 18 and 19: "As a result therefrom, confluent endothelial layer having a high quality is formed." This language now appears also in new claims 26 and 29. In contrast the reference Chamberlain states on page 8, lines 13 and 14: "Some cell detachment is observed in tials, but better than 80 % of the cells are retained." In view of this language of the Chamberlain reference, claims 26 and 29 clearly define over the teaching of the Chamberlain reference.

It is decisive according to the present application that the shearing forces increased up to physiological values, that is the shearing forces reach values as they are present in the lab circulation of a human being. The range of shearing forces is set forth for example on page 9, line 5 of the applicants' specification. This range is now claimed specifically in claims 25 and 28. Shearing forces reaching physiological values present in the blood circulation of a human being are not present in the Chamberlain teaching. New claims 25 and 28 recite specific values for the shearing forces employed according to the present invention and thereby distinguish patentably over the Chamberlain reference.

Claims 1-18 are written as product-by-process claims, and according to MPEP § 2113, these claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production, but on the product itself. Therefore, patentable weight is given only to the structural limitations of the cardiovascular prosthesis itself and not to the method or apparatus for forming the confluent monolayer of endothelial cells on the surface of the cardiovascular implant.

The Office Action is concerned about the product by process claims of the applicant. The product is characterized by the kind and the way of its production, that is the growth of the endothel cells under shearing stress. Applicant urges that this feature is not only a method feature, but also a structural feature. The protheses according to the present invention are clearly distinguished from those protheses, where the growth of the endothel cells is not performed under permanent action of shearing stress. Applicants' process results in a confluent endothelial layer having a high quality, which is clearly not a feature of the Chamberlain products.

Claims 17-21, see Figure 3 and pages 6-7, lines 29-2 for method and apparatus for forming a confluent inonolayer of endothelial cells on the surface of the cardiovascular implant.

Applicants urge that the method of claim 17 and the method steps of claim 27 are clearly outside the scope of the teaching of the Chamberlain reference.

Entry of claims 21 through 29 is respectfully requested.

Reconsideration of all outstanding rejections is respectfully requested.

Respectfully submitted,

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MARKED-UP VERSION OF THE AMENDED CLAIMS

(Version with marking to show changes made)

8. (amended) Cardiovascular prostheses according to claim 6, characterized in that the outer perfusion circuit (5') can be operated by a method selected from the group consisting of [in] co-current transporting to the inner perfusion circuit (5), [or in] counter-current transporting to the inner perfusion circuit (5), [but also statically] and static transporting to the inner perfusion circuit (5)..

13. (amended) Cardiovascular prostheses according to claim 6, characterized in that the realization of the adapters (3, 3') for fixing the prosthesis (1) [can be] is realized [as] by an olive [, cones with clamping means or as an expansion member].

16. (amended) Cardiovascular prostheses according to claim 1, characterized in that the prosthesis is used as a member selected from the group consisting of a vascular prosthesis, a heart valve prosthesis [or] and a stent.

20. (three times amended) The method according to claim 17, characterized in that

a) the outer perfusion circuit (5') can be operated in co-current or counter-current to the inner perfusion circuit (5), but also statically,

b) the two perfusion circuits (5, 5') do not work as a closed system but lead from one medium reservoir (6) into another medium reservoir (6'), in which the medium collected has already streamed through the prosthesis,

c) the inner and the outer perfusion circuits have a member selected of the group consisting of different medium reservoirs [or] and one and the same medium reservoir (6, 6'), and

d) the two perfusion circuits (5, 5') unite inside the chamber (2) after having streamed the prosthesis (1), but leave the chamber (2) in separate perfusion circuits (5, 5').

22. (new) Cardiovascular prostheses according to claim 6, characterized in that the realization of the adapters (3, 3') for fixing the prosthesis (1) is realized by cones with clamping means.

23. (new) Cardiovascular prostheses according to claim 6, characterized in that the realization of the adapters (3, 3') for fixing the prosthesis (1) is realized by an expansion member.

24. (new) Cardiovascular prostheses comprising

an endothelial cell surface produced wherein the formation of a confluent monolayer ensues by the cells growing under a permanent influence of defined pulsatile shear forces increasing up to physiological values after an initial sub-confluent seeding of a surface on the blood contact side, by means of streaming the prosthesis surface on the blood contact side along a main axis of the prosthesis in an inner perfusion circuit and by moistening an outer prosthesis wall in an outer perfusion circuit, or in a permeable medium reservoir.

25. (new) The cardiovascular prostheses according to claim 24 wherein the shear force is from about 0.01 to 5 dyn/cm2.

26. (new) The cardiovascular prostheses according to claim 24 wherein a confluent endothelial layer having a high quality is present.

27. (new) A method for covering cardiovascular prostheses with endothelial cells comprising the following steps:

initially sub-confluently seeding the prosthesis surface on the blood contact side;

streaming the prosthesis surface on the blood contact side along the main axis of the prosthesis in an inner perfusion circuit, and a moistening of the outer prosthesis wall in an outer perfusion circuit or in a permeable medium reservoir;

growing cells growing under a permanent influence of defined pulsatile shear force increasing up to physiological values;

forming a confluent monolayer of the grown cells.

28. (new) The method for covering cardiovascular prostheses according to claim 27 further comprising

employing a shear force from about 0.01 to 5 dyn/cm2.

29. (new) The method for covering cardiovascular prostheses according to claim 27 further comprising

forming a confluent endothelial layer having a high quality.